

# Investigation of the treatment and follow-up approaches of pregnant with asthma

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## ABSTRACT

**Aims:** Uncontrolled asthma during pregnancy can lead to complications for both the mother and the fetus. In this study; It was aimed to evaluate the follow-up and treatment of pregnant women with asthma, their knowledge about asthma triggers, their use of inhaler therapy, and their compliance with pulmonologist controls for asthma.

**Methods:** In this study; 64 pregnant patients with asthma who applied to our clinic between 01.01.2022 and 31.07.2022 were reviewed. Demographic patients (mean age, age groups, smoking history, comorbidities), recommended treatment information, and birth information, whether they used asthma treatment or not, were recorded and evaluated according to patient groups.

**Results:** There was a statistically significant difference between drug use during pregnancy according to the age groups of pregnant women with asthma (Chi-square test;  $\chi^2=6.684$ ;  $p=0.035$ ). As the age of the pregnant women increased, the rate of drug use during the pregnancy increased, and there was a correlation between drug use during pregnancy and whether the patients were regularly checked by a pulmonologist (Chi-square test;  $\chi^2=12.835$ ;  $p=0.0001$ ). While 68% of those who were not under the control of a pulmonologist did not use medication, 60.8% of those under the control of a pulmonologist used medication during their pregnancy.

**Conclusion:** Pregnant women with asthma must be followed by a gynecologist and a pulmonologist. Using inhaler therapy in asthma treatment in pregnant women can keep asthma under control and reduce the number and severity of exacerbations.

**Keywords:** Pregnancy, asthma therapy, inhaler therapy, asthma triggers

## INTRODUCTION

Asthma is one of the most common chronic diseases in pregnancy. Epidemiological studies showed that approximately 4% of all pregnancies are complicated by asthma. In addition, life-threatening asthma or status asthmaticus has been reported in 0.05% to 2% of all pregnancies. Uncontrolled asthma during pregnancy can lead to both maternal and fetal complications. The relationship between asthma and pregnancy is not one-sided because not only does uncontrolled asthma cause morbidity in the mother and the baby, but pregnancy also increases bronchial inflammation, impairing asthma control and making attacks more frequent. As a classical knowledge, asthma shows a variable course during pregnancy. In 1/3 of asthmatics, asthma worsens with pregnancy, remains stable in 1/3, and may improve in 1/3. A study showed that the disease worsened in 52-65% of pregnant women with severe asthma, and worsening occurred in only 8-13% of pregnant women with mild asthma.<sup>1</sup>

The effect of pregnancy on asthma can have variable results. Deterioration in asthma control usually begins in the second trimester of pregnancy. It manifests as wheezing, decreased sleep quality, and difficulty in daily activities. Exacerbations also usually increase in the second trimester. Drug use increases compared to the first trimester and is at the highest level in the third trimester. In 60% of consecutive pregnancies, asthma progresses during the first pregnancy. It is stated that allergen exposure does not cause a different worsening in pregnant asthmatics. It has been reported that diseases accompanying asthma, such as allergic rhinitis, have a similar course at a rate of 50% during pregnancy.<sup>2</sup>

Viral infections can cause uncontrolled asthma in pregnant asthmatics. Preventing upper respiratory tract viral infections in pregnant women is very important for asthma control. Smoking and addiction to inhaled steroids are other factors that complicate asthma control during pregnancy.<sup>3</sup>

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Prolonged pregnancy, preterm delivery, preeclampsia, high perinatal mortality, elective cesarean section, low birth weight, and risk of congenital malformations are common potential complications. Low birth weight babies increase by 46%, preterm birth by 22%, and preeclampsia by 54% in pregnant women with asthma. The incidence of cleft lip with or without cleft palate increases compared to pregnant women without asthma. While there is almost no maternal or fetal impact in pregnant women with mild or moderate asthma, the risk is higher in severe asthma.<sup>2,3</sup>

Asthma is a fairly common health problem for pregnant women and a potentially serious medical condition that can complicate pregnancy. Many complications are related to the lack of disease control, which can negatively affect the mother's quality of life and perinatal outcomes. The course of asthma symptoms during pregnancy is unpredictable, but exacerbations are more common in the second trimester. The causes are multifactorial, and the asthma phenotype may play a role. It has been suggested that CARAT (Allergic Rhinitis and Asthma Test Control) and pulmonary function tests can be used to monitor and adjust treatment during pregnancy in patients with asthma. Uncontrolled asthma causes many maternal and fetal complications, such as hyperemesis, hypertension, pre-eclampsia, antepartum or postpartum vaginal bleeding, placenta previa, cesarean delivery, delivery complications, intrauterine growth retardation, premature birth, low birth weight, increased perinatal mortality, and neonatal hypoxia.<sup>2</sup>

Within the scope of this research, we aimed to elucidate the follow-up treatments for pregnant women with asthma and to evaluate the effects of the drugs used on the fetus and the mother, the factors that trigger asthma, and the use of the correct inhaler. Asthma during pregnancy must be kept under control to prevent both maternal and fetal complications. For control, the pregnant woman must know the treatment and follow-ups of asthma, the triggering factors of asthma, and the correct use of inhaler medications used in treatment.

## METHODS

The sample size was determined as 102 pregnant women with asthma who applied to outpatient our clinic of Şişli Hamidiye Etfal Training & Research Hospital between 01.01.2022 and 31.07.2022. 102 patients were randomly selected for the study, but only the data of 64 of the patients could be reached completely and these patients were included in the study. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. The study was initiated with the approval

of the University of Health Sciences Şişli Hamidiye Etfal Training and Research Hospital Clinical Researches Ethics Committee (Date: 20.09.2022, Decision No: 3669). As this was a retrospective analysis, no informed consent has been obtained from participants.

Demographics (age, smoking history), comorbidities, asthma diagnosis information (old diagnosis or diagnosis made during pregnancy), treatment information used before and during pregnancy, patients' information about asthma triggers during pregnancy, and information on whether patients use their inhalers correctly during pregnancy. Whether the pregnant women were under the control of a pulmonologist or not and the birth information of the patients were obtained from hospital records.

### Inclusion Criteria

Pregnant individuals  $\geq 18$  years old, who were diagnosed with asthma have been included in this analysis.

### Exclusion Criteria

Women under the age of 18 who do not have any respiratory symptoms, those who have a psychiatric disease that prevents them from using inhalers, and pregnant women who are not diagnosed with asthma.

### Statistical Analysis

Patient data collected within the scope of the study were analyzed with the IBM Statistical Package for the Social Sciences (SPSS) for Windows 23.0 (IBM Corp., Armonk, NY) package program. Frequency and percentage for categorical data and mean and standard deviation for continuous data were given as descriptive values. For comparisons between groups, the "Independent Sample T-test" was used for two groups, and the "Pearson Chi-Square Test" was used to compare categorical variables. The results were considered statistically significant when the p-value was less than 0.05. Considering the difference in the medium effect size (effect size=0.5) between the groups, the sample size was calculated as 102 patients for the alpha significance level 0.05 and 80% Power (Sample size was calculated with the G\*Power Version 3.1.6 program).

## RESULTS

38 (59.37%) were in the age group of 19 – 29, 21 (32.81%) were in the age group of 30 – 39, and 5 (7.82%) were 40 and over. 12 (18.75%) of the patients are smokers, 24 (37.5%) are ex-smokers and 28 (43.75%) are non-smokers. 53 (82.82%) patients had a previous diagnosis, and 11 (17.18%) patients had a new diagnosis. 27 (42.18%) had allergic rhinitis, 6 (9.37%) had obesity, 7 (10.93%) had diabetes mellitus (DM), 5 (7.18%) had a cardiovascular disease, 3 (4.68%) had hypertension, 1 (1.56%) had epilepsy and 15 (24.10 %) (**Table 1**).

**Table 1.** Demographic characteristics of patients (age, smoking status, comorbidities, asthma diagnosis status)

| Variables              | n  | %     |
|------------------------|----|-------|
| Age                    |    |       |
| 19-29 Years            | 38 | 59.37 |
| 30-39 Years            | 21 | 32.81 |
| 40≤                    | 5  | 7.82  |
| Smoking status         |    |       |
| Smoker                 | 12 | 18.75 |
| Ex-smoker              | 24 | 37.50 |
| Non-smoker             | 28 | 43.75 |
| Comorbidities          | 27 | 42.18 |
| Allergic Rhinitis      | 6  | 9.37  |
| Obesity                | 7  | 10.93 |
| Diabetes Mellitus      |    |       |
| Cardiovascular Disease | 5  | 7.18  |
| Hypertension           | 3  | 4.68  |
| Epilepsy               | 1  | 1.56  |
| None                   | 15 | 23.43 |
| Asthma Diagnosis       |    |       |
| New                    | 11 | 17.18 |
| Old                    | 53 | 82.82 |

62.50% used salbutamol, 39.06% used antihistamines, and 26.56% used long-acting beta- agonists (LABA) in combination with inhaled corticosteroid (ICS). 25.0% of patients had an episiotomy, 43.75% had a cesarean section, 1.56% had a breech delivery, and 29.68% experienced a normal vaginal birth. 42.18% of patients were followed by a pulmonologist, while the remaining 57.82% were not. Among the patients, 35.94% used an inhaler, while 64.06% did not. 14.06% of patients did not attend their follow-up appointments and instead relied solely on their asthma medications. 39.06% of patients used medication for allergic rhinitis (**Table 2**).

**Table 2.** The characteristics of the type of birth and drug use during pregnancy

| Variables                       | n  | %     |
|---------------------------------|----|-------|
| Medications used                |    |       |
| Antihistaminic drug             | 25 | 39.06 |
| Salbutamol                      | 40 | 62.50 |
| LABA+ICS                        | 17 | 26.56 |
| Delivery Mode                   |    |       |
| Episiotomy                      | 16 | 25    |
| Cesarean section                | 28 | 43.75 |
| Normally birth                  | 19 | 29.68 |
| Breech birth                    | 1  | 1.56  |
| Pulmonologist follow-up         |    |       |
| No                              | 37 | 57.81 |
| Yes                             | 27 | 42.19 |
| Medication use during pregnancy |    |       |
| No                              | 41 | 64.06 |
| Yes                             | 23 | 35.94 |

LABA: long affective beta-2 mimetic agonist, ICS: İnhaler corticosteroid

32 (50%) patients had allergies and/or were aware of their triggers. These patients 3 (4.68%) had a prick test (+) (**Table 3**). Significant differences in drug use patients based

on their age groups were observed ( $\chi^2=6.684$ ;  $p=0.035$ ) (**Table 4**). 27 (42.12%) were controlled by a pulmonologist and 23 (35.88%) were using medications in pregnancy. There was a significant difference in the medication use of pregnant women with asthma depending on whether they were treated by a pulmonologist or not. (Chi-square test;  $\chi^2=12.835$ ;  $p=0.0001$ ). While 68% of those who were not controlled by a pulmonologist did not use a drug, 60.8% of those who followed a pulmonologist were used in pregnancy (**Table 5**). 23 patients who used inhaler therapy, 18 used it correctly (**Table 6**).

**Table 3.** Understanding asthma triggers based on age in pregnant women with asthma

| Understanding asthma triggers during pregnancy | No         | Yes        | no attention |
|------------------------------------------------|------------|------------|--------------|
| Age                                            |            |            |              |
| 19-29                                          | 21 (55.3%) | 17 (44.7%) | 24 (63.1%)   |
| 30-39                                          | 10 (47.6%) | 11 (52.4%) | 10 (47.6%)   |
| 40≤                                            | 1 (20%)    | 4 (80%)    | 2 (40%)      |
| Total                                          | 32 (50%)   | 32 (50%)   | 36 (56.2%)   |

**Table 4.** Examining drug use during pregnancy among pregnant women with asthma across different age groups

| Medication use during pregnancy | No         | Yes       | Total      |
|---------------------------------|------------|-----------|------------|
| Age                             |            |           |            |
| 19-29                           | 19 (61.3%) | 2 (22.2%) | 21 (52.5%) |
| 30-39                           | 12 (38.7%) | 6 (66.7%) | 18 (45%)   |
| 40≤                             | 0 (0%)     | 1 (11.1%) | 1 (2.5%)   |
| Total                           | 31         | 9         | 40         |

Chi-square test;  $\chi^2=6.684$ ;  $p=0.035$

**Table 5:** Whether pregnant women are under the care of a pulmonologist affects their drug use.

| Pulmonologist follow-up         | No        | Yes        | Total      |
|---------------------------------|-----------|------------|------------|
| Medication use during pregnancy |           |            |            |
| No                              | 21 (100%) | 10 (52.6%) | 31 (77.5%) |
| Yes                             | 0 (0%)    | 9 (47.4%)  | 9 (22.5%)  |
| Total                           | 21        | 19         | 40         |

Chi-square test;  $\chi^2=12.835$ ;  $p=0.0001$

**Table 6:** According to prenatal Pulmonologist consultation, the correct use of inhalers according to the age groups of pregnant women

| Inhaler use during pregnancy | Inhaler using | Correct inhaler using |
|------------------------------|---------------|-----------------------|
| Age                          |               |                       |
| 19-29                        | 10 (15.6%)    | 9 (14.1%)             |
| 30-39                        | 9 (14.1%)     | 7(10.9%)              |
| 40≤                          | 4 (6.2%)      | 2 (3.1%)              |
| Total                        | 23 (35.9%)    | 18 (28.1%)            |

## DISCUSSION

We retrospectively evaluated the files of 64 pregnant women with asthma aged 19-47 who gave birth in our hospital. Over half of them were under 30, and 18.75% of them continued to smoke during pregnancy. Women over 30 with asthma face high-risk pregnancies, and if not managed properly, it can lead to premature birth and low birth weight.<sup>2,3</sup> 27 (42.18%) of patients had allergic rhinitis and asthma. 7 (10.93%) patients had diabetes

mellitus (DM) as a common comorbidity. Up to 65% of pregnant women may experience nasal symptoms that can vary in control. Vasomotor rhinitis of pregnancy is likely if symptoms occur in the second or third trimester and resolve within 5 days after giving birth.<sup>1,2-4</sup>

In the study, 25% had an episiotomy, 43.75% had a cesarean section, 1.56% had a breech delivery, and 29.68% had a normal vaginal birth. Severe asthma attacks occur between the 24<sup>th</sup> and 36<sup>th</sup> weeks of pregnancy, but 90% of asthmatics have no complications during delivery. Emergency visits are reported in 11-18% of pregnant women with asthma, and hospitalization in 62%. It is crucial to control asthma during pregnancy for the health of both the mother and baby. Hypoxia can affect the baby's growth, so managing asthma carefully during pregnancy is important.<sup>2,6</sup>

Our study found that 82.82% of patients had asthma prior to pregnancy, while 17.18% were diagnosed during pregnancy. Asthma causes coughing, wheezing, chest tightness, and shortness of breath. Symptoms can worsen at night and be triggered by allergens, infections, smoke, exercise, and irritants. A physical examination and detailed medical history can help diagnose asthma. Pregnant women can experience similar symptoms due to body changes, which can decrease lung function. Therefore, a careful diagnosis is necessary to differentiate between pregnancy-related symptoms and asthma.<sup>7,8</sup>

Our study found that 42% of patients were under the care of a pulmonologist, while 36% used inhalers. 14% of patients did not attend follow-up appointments but still used their asthma medications. 39% of patients used medication for allergic rhinitis during pregnancy. Most pregnant patients used short-acting beta 2-agonist (SABA) salbutamol. Recent studies have shown that a fixed combination of LABA and low-dose ICS can be used as first-line therapy for mild asthma. This combination can be used as both maintenance and reliever therapy (MART) if necessary to control asthma symptoms. MART has been proven to be effective in managing asthma and can lead to lower overall use of ICS and fewer exacerbations. SABA can be used as a reliever therapy, but only in combination with maintenance ICS and LABA if needed.<sup>3</sup>

There is a low chance of fetal malformation caused by inhaled SABA. During delivery, systemic SABA may have a tocolytic effect. It is important to note that LABA should never be prescribed as a reliever or maintenance therapy without ICS. If LABA is needed to control asthma, it should be used in combination with ICS. The available data on the effects of LABA on the fetus is limited, but it is encouraging. The use of low and moderate doses of ICS during pregnancy has not been linked to an increased risk of malformations, preterm birth, low birth weight,

or SGA. However, it is hard to determine if higher doses are associated with adverse events or if these events are due to the severity of the underlying disease and/or the frequency of exacerbations. On the other hand, some studies suggest that the use of systemic steroids in pregnant women during the first trimester may increase the risk of cleft lip, cleft palate, premature birth, low birth weight, and preeclampsia.<sup>3</sup>

Salmeterol has the longest safety record and can be utilized in conjunction with ICS (ICS/LABA) as a maintenance therapy, along with SABA as required. Other LABAs in combination with ICS can also be considered, particularly in situations where adherence may be a concern.<sup>3</sup>

What do pregnant women know about asthma triggers according to their age groups? Half of the patients with asthma, allergies, and drug allergy reactions were aware of the triggers that caused their symptoms. Specific immunoglobulin E (IgE) levels in the patient's peripheral blood can help determine which allergens are causing symptoms. To manage symptoms, patients should avoid known allergens by using dust mite covers, removing pets, and exterminating cockroaches. While subcutaneous immunotherapy is not usually started during pregnancy, it may be continued at the same dose as before pregnancy if the patient was already at maintenance dosing. However, sublingual immunotherapy is not recommended during pregnancy.<sup>9</sup>

Pregnant women with asthma tend to use more drugs during pregnancy as they age. To have a safe pregnancy, they should avoid triggers and tobacco exposure, and take their asthma medication properly. Induction of labor is not commonly recommended due to asthma, as moderate to severe asthmatic patients tend to have a higher planned cesarean section rate. Obstetricians and respiratory physicians have teamed up to prevent serious complications during labor for pregnant women with asthma. This collaboration reduced severe respiratory issues during labor from 72 to 14 per 10,000 deliveries with asthma between 2000 and 2018. However, women with asthma who attempt vaginal delivery may have a higher risk of emergency caesarean section deliveries (OR 1.29) due to increased respiratory symptoms and complications related to maternal asthma.<sup>3</sup>

A study on 27 pregnant women with asthma found that medication use was significantly higher among those who were monitored by a pulmonologist. Asthma during pregnancy has been linked to severe maternal morbidity. In a prospective study, 23% of women with asthma improved, while 30% worsened. Among women with mild asthma, 12.6% had exacerbations and 2.3% required hospitalization.

Asthma during pregnancy has been linked to severe maternal morbidity. Among pregnant women with



asthma, 23% improved and 30% worsened. Women with asthma had an increased risk of low-birth-weight babies, pre-eclampsia, and preterm birth, compared to those without asthma. A meta-analysis revealed a statistically significant increase in the risk of non-major congenital malformations in women with asthma.<sup>10</sup> Asthmatic pregnant women have a higher rate of perinatal mortality. Proper asthma treatment before pregnancy is crucial to prevent spontaneous abortion. Women who experienced an asthma attack during pregnancy had a higher rate of low-birth-weight babies and were three times more likely to have a baby with low birth weight compared to those who did not have an attack. Enrolling in an asthma management program and monitoring disease activity during pregnancy can lead to better adherence with ICS. Asthmatics under optimal control during pregnancy did not experience ante-natal complications. Pregnant women with asthma are high-risk patients. Uncontrolled asthma can harm the mother and fetus. Proper asthma management ensures a good prognosis. Asthma exacerbations during pregnancy can cause harmful hypoxia for the fetus. Administer the lowest possible dose of medication to minimize fetal risk. Avoid multiple drug administration, especially in the first trimester.<sup>16</sup> In addition to the general pharmacological treatment principles for the treatment of asthma in pregnant women, the following points should be considered: 1) maternal symptoms and fetal development should be monitored objectively 2) environmental asthma-inducing factors should be well controlled, 3) patient education should be as little as drug therapy. great importance should be given.<sup>17,18</sup>

## CONCLUSION

Asthma treatment in pregnant women is still difficult due to the physiological conditions of asthma and pregnancy. Pregnant asthmatics should be followed up with a gynecologist and chest disease specialist. Treatment aims to keep asthma under control and reduce the number and severity of exacerbations. In this way, possible fetal risks can be prevented. The education of the pregnant, the rescue and therapeutic drugs to be used at home, the way of use should be taught, and preparation for birth should be ensured with regular controls.

Managing asthma during pregnancy can be challenging due to the unique physiological conditions of both asthma and gestation. The study suggests a collaborative approach between gynecologists and pulmonologists to achieve optimal asthma control during pregnancy. Education, proper medication usage, and regular follow-up appointments are vital components of successful asthma management in pregnant women.

## ETHICAL DECLARATIONS

### Ethics Committee Approval

The study was initiated with the approval of the University Şişli Hamidiye Etfal Training and Research Hospital University Medical Faculty Clinical Researches Ethics Committee (Date: 20.09.2022, Decision No: 3669).

### Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

### Referee Evaluation Process

Externally peer-reviewed.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Financial Disclosure

The authors declared that this study has received no financial support.

### Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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